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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/899,276	ROESL ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 6/24/04. The amendment has been entered. New claims 16-20 have been added. Claims 1-20 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

Claims 11-15 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/23/03.

This application contains claims 11-15, drawn to an invention nonelected with traverse in the Paper filed 12/23/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-10 and 16-20 are examined herein.

Sequence Compliance

The specification has been amended such that the disclosed sequences have been assigned an appropriate SEQ ID NO. As such, the objection to the specification for not being in compliance with the sequence rules has been withdrawn.

Claim Objections

Claims 1-10 and 16-20 are objected to because of the following informalities: independent claims 1 and 10 recite the phrase "the protein encoded by the nucleic acid sequence of EMBL Accession No. Y18933". It is respectfully pointed out that this is an improper way to reference a sequence. Any sequence reference should include a sequence identifier (i.e., SEQ ID NO) as set forth in 37 C.F.R. § 1.821-1.825. It is acknowledged that the scope of enablement rejection set forth in the previous rejection, and reiterated herein, refers to the nucleic acid sequence using the same Accession number. This is due to the fact that the specification does not disclose the actual nucleic acid sequence encoding MCP-1, nor is the nucleic acid sequence encoding MCP-1 disclosed in the paper sequence listing (or CRF). The only reference to the nucleic acid sequence encoding MCP-1 is the indicated Accession No., therefore, that was the only means by which the Examiner could identify the nucleic acid sequence. In order to refer to the nucleic acid sequence encoding MCP-1 properly, applicants may have to amend the specification to enter the actual nucleic acid sequence (if the actual sequence is not disclosed in the present application). Should applicants have to amend the specification to enter the sequence of the nucleic acid encoding MCP-1, a new paper listing and CRF is also required. Furthermore,

a proper oath/declaration would have to be filed along with evidence that indicates that applicants were in possession of nucleic acid sequence encoding MCP-1 at the time of filing.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

The claims have been amended to indicate that the nucleic acids are isolated nucleic acids. As such, the claims do not read on non-statutory subject matter and the rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 remains rejected and new claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.

It is noted that claim 1 has been amended. However, amended claim 1 (as well as new independent claim 16) encompass an isolated nucleic acid comprising a nucleic acid sequence encoding the MCP-1, including "fragments, derivatives or allelic variants of said sequence which encode a polypeptide having the biological activity of MCP-1 and an "amino acid sequence

identity of at least 80% to the amino acid sequence encoded (by) the EMBL clone Y18933" and at least one hypersensitive region.

Therefore, the claims are drawn to a genus of molecules (i.e., nucleic acids) wherein the molecules encompass any nucleic acid sequence that encodes a polypeptide having the biological activity of MCP-1 and that is 80% identical to the sequence encoding MCP-1, including all fragments, derivatives and allelic variants that have the biological activity. This genus of molecules encompasses possibly thousands of different nucleic acid molecules, considering every possibly fragment, derivative and allelic variant encompassed by the claims. Furthermore, it is noted that the specification (as well as the prior art) does not disclose the critical elements of MCP-1 such that one of skill in the art would know which derivatives, fragments and variants would have biological activity without doing additional experimentation.

As previously indicated, The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164).

Since the specification and prior art do not describe any structure–function relationship for the molecules encompassed by the claims, additional experimentation would be required in order for one of skill in the art to be able to know which fragments, derivatives and allelic

variants encompassed by the claims actually had MCP-1 biological activity, and which fragments, derivatives and allelic variants did not have MCP-1 biological activity. Therefore, applicants have not sufficiently described the genus of nucleic acid sequences that are encompassed by the claims. It is noted that a review of the prior art did indicated that there are at least two sequence homologues, one encoding mouse JE and another encoding human JE (e.g., see Rollins et al., MCB 1998), however, the sequence structures of these homologues which are critical to conferring the biological activity of MCP-1 to the proteins are not described. Therefore, there is an insufficient description of the nucleic acid sequences encompassed by the claims.

It is noted that claims 2-10 and 17-20 are dependent claims that depend on either claim 1 or claim 16. The dependent claims encompass all of the limitations of the independent claims; therefore, claims 2-10 and 17-20 are rejected for the same reasons.

Additionally, claims 1-10 and 16-20 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A nucleic acid molecule comprising: (a) a nucleic acid sequence encoding MCP-1, wherein the MCP-1 protein is the protein encoded by the nucleic acid sequence of EMBL Accession No. Y18933; and (b) a 5'-DHSR or 3'-DHSR wherein said 5'DHSR contains the nucleic acid sequence that is SEQ ID NO: 4, 5, or 6 and wherein said 3'-DHSR comprises the nucleic acid sequence that is TGAGTCA, or SEQ ID NO: 1, 2, 3, or 8;

does not reasonably provide enablement for the full scope of the claims—such as a nucleic acid comprising a nucleic acid sequence encoding a protein having the biological activity of MCP-1, and 5'-DHSRs or 3'DHSRs that do not explicitly comprise TGAGTCA or SEQ ID NO. 1 or SEQ ID NO. 8. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As mentioned above, the claims encompass sequences for which there is insufficient written description provided in the specification and include sequence homologues as well as functional homologues which may have completely different structures from the disclosed sequences. Without a clear indication of the minimal critical elements that are required to confer MCP-1 biological activity to a protein, the written description requirements have not been sufficiently met. As such, one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation in order to first properly identify a representative number of species encompassed by the claims.

Claims 1, 5 and new claims 16, 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As mentioned above, the Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying

characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164).

The instant claims are drawn to a nucleic acid as indicated in claim 1(b) and claim 16(b) wherein the hypersensitive sequences contain mutations resulting in a modified DNAse 1 hypersensitivity, S1 hypersensitivity, and/or altered interaction with a transcription factors and wherein the mutated sequence is 40% identical to the original sequence. Therefore, the claims encompass a genus of molecules which is indeterminate in size, but could encompass thousands of different species, considering all of the mutations that are 40% identical to the original sequence and which would result in a modified hypersensitivity and/or interaction with transcription factors. Since the specification and prior art does not disclose a representative number of mutations that are 40% identical to the original sequence and which modify DNAse I hypersensitivity, S1 hypersensitivity and/or altered interaction with transcription factors, the written description requirement has not been met. That is, since the specification and prior art has not disclosed which 60% of the sequence of the 5' and 3'DHSRs can mutated such that the mutation results in the desired effect, additional experimentation would be required in order to determine which mutated sequences meet the limitations of the claim and are functional or non-functional (i.e., one would have to determine which mutations resulted in functional sites and which mutations resulted in non-functional sites). Thus the specification has not met the requirements set forth in the guidelines.

It is noted that claims 5 and 17 are dependent claims that depend on claims 1 and 16. Therefore, claims 1 and 16 must be broad enough to encompass the limitations of dependent claims 5 and 17, respectively. As such, the rejection is applicable to claims 1, 5, 16 and 17.

Additionally, claims 1, 5, 16 and 17 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A nucleic acid molecule comprising: (a) a nucleic acid sequence encoding MCP-1, wherein the MCP-1 protein is the protein encoded by the nucleic acid sequence of EMBL Accession No. Y18933; and (b) a 5'-DHSR or 3'-DHSR wherein said 5'DHSR contains the nucleic acid sequence that is SEQ ID NO: 4, 5, or 6 and wherein said 3'-DHSR comprises the nucleic acid sequence that is TGAGTCA, or SEQ ID NO: 1, 2, 3, or 8;

does not reasonably provide enablement for the full scope of the claims—such as a nucleic acid comprising a nucleic acid sequence encoding a protein having the biological activity of MCP-1, and 5'-DHSRs or 3'DHSRs that have mutations that result in DNAse I hypersensitivity, S1 hypersensitivity, or altered interaction with transcription factors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. As mentioned above, the claims encompass mutations for which there is insufficient written description provided in the specification. Without a clear indication of the mutations that confer hypersensitivity/altered transcription factor binding, the written description requirements have not been sufficiently met. As such, one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation in order to first properly identify a representative number of species encompassed by the claims.

It is noted that claims 5 and 17 depend on claims 1 and 16, respectively. Therefore, claims 1 and 16 must be broad enough to encompass the limitations of claims 5 and 17. As such, the rejection is proper for claims 1, 5, 16 and 17.

Response to Arguments

Applicant's arguments filed 6/24/04 have been fully considered but they are not persuasive.

With respect to the rejection of claims for not meeting the written description requirement as it pertains to fragments, derivatives and allelic variants of a nucleic acid encoding MCP-1, applicants argue that the claims have been amended to reference the specific and published sequences in the claims (see p. 12 of the response filed 6/24/04). Further, applicants argue that the claims have been amended to "clearly define the sequence variants by reference to hybridization as well as the degree of homology. Applicants refer to page 3-4 of the specification for support of a description of the sequences (see p. 12 of the response).

In response, it is respectfully pointed out that the claims have been amended to specifically encompass fragments, derivatives and allelic variants of a nucleic acid encoding MCP-1 (e.g., see claim 1 and claim 16). Furthermore, the rejection is not a new matter rejection. It is acknowledged that the specification (p. 3-4) discloses the genus of sequence variants that are 80% identical to the nucleic acid sequence encoding MCP-1. However, the specification (and prior art) do not disclose enough data to determine which sequences that are 80% identical to the nucleic acid encoding MCP-1 would have the desired function and which ones would not have the desired function without performing additional experimentation. Since additional experimentation would be required to determine which species of molecules encompassed by the claims were functional, the specification has not met the written description requirement.

Additionally, with respect to the rejection of claims for not meeting the written description requirement as it pertains to the genus of hypersensitive/transcription factor binding

sites, applicants argue that the claims have been amended such that the claims now characterize the mutations by the degree of identity to the mutated sequence (see p. 12 of the response).

In reply, it is respectfully pointed out that although the claims have been amended to recite the degree of identity to between the mutant and the original sequence, the specification and prior art do not disclose enough information in order for one of skill in the art to determine which 60% of the sequences can be mutated and result in a sequence having the desired function (hypersensitivity or transcription factor binding). Therefore the written description requirements have not been met. As such the rejection is proper and the rejection is not withdrawn.

With respect to the enablement rejection, applicants argue that the claims have been amended to recite the published nucleic acid sequence of MCP-1 and homologs thereof. Thus, applicants assert, the claimed subject matter as amended is enabled (see p. 13 of the response).

In reply, since the amended claims are still rejected under 35 USC 112, first paragraph for not meeting the written description requirement, the instant claims are also further rejected under 35 USC 112, first paragraph as not being enabled for the full scope encompassed by the claims. That is since the claims are still rejected under written description, for the reasons discussed herein, one of skill in the art would not know how to make and use the claimed invention without performing additional experimentation. Therefore, the enablement rejection is also proper and the rejection is not withdrawn,

Claim Rejections - 35 USC § 102

Claims 1-4, 6-10, 16 and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. AC005549 (Birren et al., see sequence alignment attached. NOTE: Birren is listed in the IDS PTO-1449.), for the reasons of record, reiterated below.

Birren (Genbank Accession No. AC005549) teaches a bacterial artificial chromosome (BAC) comprising a portion of chromosome 17 that comprises SEQ ID NO. 1, as well as the genomic DNA encoding the MCP-1 gene. The Genbank data (see attached) indicates that the sequence matching SEQ ID NO. 1 is comprised in a BAC, wherein the BAC also includes a genomic sequence encoding MCP-1. Since SEQ ID NO. 1 is the 3'DHSR nucleic acid sequence from position +2430 to +3019 as depicted in Figure 6 (see claim 2), and the genomic sequence encoding human MCP-1, the BAC taught by Birren in Genbank Accession No. AC005549 thus meets the limitations of claims 1-4. It is noted that the BAC is a recombinant vector that must include all of the genomic sequences of chromosome 17 associated with the expression of MCP-1 in human cells (i.e., the regulatory elements that allow the expression of MCP-1 in eukaryotic host cells). Furthermore, the construction of the BAC would require the transformation of the BAC into bacterial cells for the propagation of the instant BAC. As such, Birren (through Genbank Accession No. AC005549) necessarily teaches all of the limitations of the instant claims.

Response to Arguments

Applicant's arguments filed 6/24/04 have been fully considered but they are not persuasive.

Applicants argue that Birren solely discloses the sequence of chromosome 17, but fails to any functional features of the sequence. Applicants argue, in particular, Birren does not disclose any stretches or regions within the sequences that re involved in the transcriptional regulation of the expression of MCP-1, such as the claimed hypersensitive sites (see p. 14 of the response).

In reply it is acknowledged that Birren does disclose a bacterial artificial chromosome (BAC) that comprises a segment of chromosome 17 that contains the genomic MCP-1 gene. It is noted that the segment of chromosome 17 taught by Birren would comprise the complete genomic sequence of the MCP-1 gene, including all regulatory sequences associated with MCP-1 such as all hypersensitive regions as well as all transcription factor binding sites. Furthermore, it is respectfully pointed out that the claims are drawn to an isolated nucleic acid sequence (a product) and that Birren teaches an isolated nucleic acid sequence which meets all of the structural elements of the claims. Since the product has all of the sequence requirements of the claim, the product must, by necessity, have all of the functional properties as well. Applicants are reminded that MPEP 2112.01 teaches, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

Here, the Office has shown a sound basis for believing that the products of the claim and the product of Birren are the same. Therefore, the rejection of claims is proper and the rejection is not withdrawn.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art unit 1635

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PRIMARY EXAMINER